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Clopidogrel Plus 21 Days of Aspirin Is Superior to Aspirin Alone Within First 24 Hours of TIA or Minor Stroke

Clinical Question

Does adding clopidogrel (Plavix) improve outcomes over aspirin alone in the early treatment of transient ischemic attack (TIA) or minor stroke?

Bottom Line

Patients with minor stroke (National Institutes of Health [NIH] Stroke Scale score ≤ 3) or TIA have a decreased risk of recurrent stroke if given aspirin plus clopidogrel vs. aspirin alone if started within 24 hours of the onset of symptoms. There was no significant increase in the risk of bleeding events, and other cardiovascular outcomes were not affected. (Level of Evidence = 1b)

Synopsis

The researchers screened 41,561 patients with stroke or TIA at 114 clinical sites in China, and ultimately included 5,170 patients in the study. Inclusion criteria were as follows: 40 years or older, acute minor ischemic stroke or TIA, and an initial treatment given within 24 hours of symptom onset. Patients with low-risk TIAs (ABCD² score < 3 points) were excluded. Patients with any evidence of hemorrhage or other serious conditions on computed tomography or magnetic resonance imaging were also excluded, as were those with a score ≥ 2 on the 6-point modified Rankin scale for disability; recent anticoagulation or a clear indication for anticoagulation; history of intracranial

hemorrhage; recent major surgery or gastrointestinal bleed; TIA or stroke caused by angiography or surgery; or severe noncardiovascular comorbidity. All patients received aspirin on day 1, with a dose range of 75 to 300 mg, chosen by the treating physician. The patients were then randomized to one of two treatment regimens: (1) clopidogrel at 300 mg on day 1, 75 mg once daily on days 2 through 90, aspirin at 75 mg on days 2 through 21, and placebo aspirin on days 22 through 90; or (2) aspirin at 75 mg and placebo clopidogrel on days 2 through 90. The median age of participants was 62 years, and 34% were women.

Groups were balanced at the start of the study. At the end of the 90-day study period, there were fewer strokes in the clopidogrel plus aspirin group than in the aspirin-only group (8.2% vs. 11.7%; $P < .001$; number needed to treat [NNT] = 29). There was a similar reduction in the likelihood of the combined outcome of stroke, myocardial infarction, or death from cardiovascular causes (8.4% vs. 11.9%; $P < .001$; NNT = 29) and ischemic stroke (7.9% vs. 11.4%; $P < .001$; NNT = 29). There were no significant differences in the likelihood of myocardial infarction, TIA, all-cause mortality, or cardiovascular mortality. There was a trend toward more mild bleeding events in the clopidogrel plus aspirin group compared with the aspirin-only group (47 vs. 39; $P = .12$), but no difference in moderate or severe bleeds (eight in the aspirin-only group vs. seven in the clopidogrel plus aspirin group).

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Inpatient (any location) with outpatient follow-up

Reference: Wang Y, Wang Y, Zhao X, et al.; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med*. 2013;369(1):11-19.

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